## REMARKS

The specification at page 72 has been amended to correct three obvious errors of a typographical nature. Support for these amendments is found in FIG. 22, and the description of FIG. 22 at page 11, lines 1-6 of the application as filed.

Claims 1, 18, and 24 are amended, and new claims 26-38 added, to more particularly point out and distinctly claim the subject matter Applicants regard as their invention. Support for the amendment to claim 1 is found at page 4, line 17-24 of the specification as filed. Support for the amendment to claim 18 is found at page 6, lines 22-25 of the specification as filed. Support for the amendment to claim 24 is found at page 4, lines 17-24 of the specification as filed.

Support for new claims 26-34, and 36-38 is found at page 4, line 31 to page 5, line 2, and at page 14, lines 1-11, of the specification as filed. Support for new claim 35 is found at page 4, lines 17-24, at page 6, lines 9-12 and 22-25, at page 13, lines 13-17, and at page 35, lines 7-11 of the specification as filed. Support for the phrase "at least a" in claims 1 and 24 is found at page 40, lines 2-6; page 41, lines 33-35; and at page 43, lines 25-28.

No new matter has been added.

## CONCLUSION

Upon entry of this Preliminary Amendment, claims 1-38 will be pending in the present application. A copy of the pending claims is attached hereto as Exhibit C.

Other than the fees calculated on the attached Amendment Fee Sheet, Applicants believe that no fee is due for this submission. However, should the Patent Office determine otherwise, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Applicants respectfully request entry and consideration of the foregoing amendments and remarks.

Respectfully submitted,

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Date: April 5, 2002

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Enclosure

## APPENDIX A
## MARKED-UP VERSION OF THE PARGRAPH AMENDED IN THE PRELIMINARY AMENDMENT FILED April 5, 2002
## U.S. PATENT APPLICATION SERIAL NUMBER 09/781,182

The procedure was repeated with U-46619 followed by p-GlcNAc. p-GlcNAc produced a concentration-dependent vasocontraction from 14 to 140 μg/ml, as indicated in Figure [23] 22. At a developed concentration of 140 μg/ml, p-GlcNAc significantly contracted aortic rings by 218 ± 21 mg of developed force ($p<0.01$ ). De-endothelialized (*i.e.* endothelium was removed by gently rolling the aortic rings over a twisted stainless steel wire covered with cotton) aortic rings were contracted by only 33 ± 12 mg of developed force. Pretreatment with an endothelin EtA receptor antagonist, JKC-301 (Cyclo[D-Asp-Pro-D-Ile-Leu- D-Trp]), Sigma Biochemicals and Reagents, St. Louis, MO) (0.5 and 1 M), significantly diminished p-GlcNac-induced vasoconstriction by 57 to 61% ($p<0.01$ ).

## EXHIBIT B

## MARKED-UP VERSION OF THE CLAIMS AMENDED IN THE PRELIMINARY AMENDMENT FILED April 5, 2002
## U.S. PATENT APPLICATION SERIAL NUMBER 09/781,182

1. (Amended) A method for achieving <u>at least a</u> transient, localized, modulation of vascular structure and/or function, comprising:

topically administering to a patient in need of said modulation, a sufficient amount of material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, [wherein the polymers are free of protein, substantially free of other organic contaminants, and substantially free of inorganic contaminants, and] wherein said administering induces at least [one] <u>a</u> transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a breached vessel,

whereby the patient experiences <u>at least a</u> transient, localized modulation of vascular structure and/or function.

18. (Amended) A biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, [free of protein, substantially free of other organic contaminants, substantially free of inorganic contaminants,] and having a molecular weight of about 10,000 daltons to about 30 million daltons.

24. (Amended) A method for treating a patient having a vascular disorder, comprising:

topically administering to a patient in need of such treatment, a sufficient amount of material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein [the polymers are free of protein, substantially free of other organic contaminants, and substantially free of inorganic contaminants, and wherein] said administering induces at least [one] <u>a</u> transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a

breached vessel, whereby the patient experiences at least a transient, localized modulation of vascular structure and/or function,

whereby said administering ameliorates said vascular condition.

26. (New) The method of claim 1, wherein said polymers are substantially free of protein.

27. (New) The method of claim 1, wherein said polymers are substantially free of organic contaminants.

28. (New) The method of claim 1, wherein said polymers are substantially free of inorganic contaminants.

29. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of protein.

30. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of organic contaminants.

31. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of inorganic contaminants.

32. (New) The method of claim 24, wherein said polymers are substantially free of protein.

33. (New) The method of claim 24, wherein said polymers are substantially free of organic contaminants.

34. (New) The method of claim 24, wherein said polymers are substantially free of inorganic contaminants.

35. (New) A pharmaceutical composition comprising a therapeutically effective amount of a biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and having a molecular weight of about 10,000 daltons to about 30 million daltons.

36. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of protein.

37. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of organic contaminants.

38. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of inorganic contaminants.

## EXHIBIT C

## THE CLAIMS THAT WILL BE PENDING UPON ENTRY OF THE PRELIMINARY AMENDMENT FILED April 5, 2002 U.S. PATENT APPLICATION SERIAL NUMBER 09/781,182

1. (Amended) A method for achieving at least a transient, localized, modulation of vascular structure and/or function, comprising:

topically administering to a patient in need of said modulation, a sufficient amount of material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said administering induces at least a transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a breached vessel,

whereby the patient experiences at least a transient, localized modulation of vascular structure and/or function.

2. The method of claim 1, wherein the physiological response comprises stimulation of endothelin-1 release.

3. The method of claim 2, wherein the endothelin-1 is released from vascular endothelial cells.

4. The method of claim 1, wherein the physiological response comprises vasoconstriction.

5. The method of claim 1, wherein the physiological response comprises reduction in blood flow out of a breached vessel.

6. The method of claim 1, wherein the poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and said polymer has a molecular weight of about 10,000 daltons to about 30 million daltons.

7. The method of claim 6, wherein the poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 50,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and said polymer has a molecular weight of about 10,000 daltons to about 10 million daltons.

8. The method of claim 7, wherein the poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 10,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and said polymer has a molecular weight of about 10,000 daltons to about 2 million daltons.

9. The method of claim 8, wherein the poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 4,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and said polymer has a molecular weight of about 10,000 daltons to about 800,000 daltons.

10. The method of claim 6, wherein the semi-crystalline poly-β-1→4 N-acetylglucosamine polymer comprises at least one N-acetylglucosamine monosaccharide that is deacetylated, and wherein at least 40% of said N-acetylglucosamine monosaccharides are acetylated.

11. The method of claim 1, wherein the patient is a human.

12. The method of claim 1, wherein the material is in the form of a gel, sponge, film, membrane, foam, spray, emulsion, suspension, or solution.

13. The method of claim 1, wherein the material is applied directly to a blood vessel.

14. The method of claim 1, wherein the vascular structure is a blood vessel selected from the group consisting of capillary, vein, and artery.

15. The method of claim 14, wherein the blood vessel is a breached blood vessel.

16. The method of claim 15, whereby the patient experiences cessation of bleeding.

17. The method of claim 1, wherein the extent of the transient, localized modulation of vascular structure and/or function is substantially proportional to the amount of semi-crystalline poly-β-1→4 N-acetylglucosamine administered.

18. (Amended) A biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and having a molecular weight of about 10,000 daltons to about 30 million daltons.

19. The material of claim 18, wherein the semi-crystalline poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 50,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation and has a molecular weight of about 10,000 daltons to about 10 million daltons.

20. The material of claim 18, wherein the semi-crystalline poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 10,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation and has a molecular weight of about 10,000 daltons to about 2 million daltons.

21. The material of claim 18, wherein the semi-crystalline poly-β-1→4 N-acetylglucosamine polymer comprises about 50 to about 4,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation and has a molecular weight of about 10,000 daltons to about 800,000 daltons.

22. The material of claim 18, wherein the semi-crystalline poly-β-1→4 N-acetylglucosamine polymer comprises at least one N-acetylglucosamine monosaccharide that is deacetylated, and wherein at least 40% of said N-acetylglucosamine monosaccharides are acetylated.

23. The material of claim 18, wherein the material is a gel, sponge, film, membrane, foam, spray, emulsion, suspension, or solution.

24. (Amended) A method for treating a patient having a vascular disorder, comprising:

topically administering to a patient in need of such treatment, a sufficient amount of material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said administering induces at least a transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a breached vessel, whereby the patient experiences at least a transient, localized modulation of vascular structure and/or function,

whereby said administering ameliorates said vascular condition.

25. The method of claim 24, wherein the vascular disorder is selected from the group consisting of menorrhagia, cerebral aneurysm, abdominal aneurysm, uterine fibroid lesion, and blood vessel puncture.

26. (New) The method of claim 1, wherein said polymers are substantially free of protein.

27. (New) The method of claim 1, wherein said polymers are substantially free of organic contaminants.

28. (New) The method of claim 1, wherein said polymers are substantially free of inorganic contaminants.

29. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of protein.

30. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of organic contaminants.

31. (New) The biodegradable, non-barrier forming material of claim 18, wherein said polymers are substantially free of inorganic contaminants.

32. (New) The method of claim 24, wherein said polymers are substantially free of protein.

33. (New) The method of claim 24, wherein said polymers are substantially free of organic contaminants.

34. (New) The method of claim 24, wherein said polymers are substantially free of inorganic contaminants.

35. (New) A pharmaceutical composition comprising a therapeutically effective amount of a biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides covalently attached in a β-1→4 conformation, and having a molecular weight of about 10,000 daltons to about 30 million daltons.

36. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of protein.

37. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of organic contaminants.

38. (New) The pharmaceutical composition of claim 34, wherein said polymers are substantially free of inorganic contaminants.